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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/905,212	07/13/2001	Venkatraman Ramakrishnan	256602000600	3863
29933	7590	02/24/2004	EXAMINER	
PALMER & DODGE, LLP KATHLEEN M. WILLIAMS 111 HUNTINGTON AVENUE BOSTON, MA 02199				LY, CHEYNE D
ART UNIT		PAPER NUMBER		
1631				

DATE MAILED: 02/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/905,212	RAMAKRISHNAN ET AL.	
	Examiner Cheyne D Ly	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 26 November 2003.

2a) This action is FINAL.                  2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-20 is/are pending in the application.

4a) Of the above claim(s) 5,6,8-11 and 14-20 is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-4,7,12 and 13 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) 1-20 are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. §§ 119 and 120

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) All b) Some \* c) None of:  
1. Certified copies of the priority documents have been received.  
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

13) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) The translation of the foreign language provisional application has been received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

#### Attachment(s)

1) <input type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ .
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .	6) <input type="checkbox"/> Other: _____ .

**DETAILED ACTION**

1. Applicant's arguments filed November 26, 2003 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.
2. The new title has been accepted.
3. Claim 7 has been rejoined with claims 1-4, 12, and 13; therefore, claims 1-4, 7, 12, and 13 are examined on the merits.
4. This is a NON-FINAL Office Action.

**PRIORITY**

5. Acknowledgment is made of applicant's claim for foreign priority based on applications filed in the United Kingdom. Further, the priority benefit to United Kingdom applications (0017376.5, 0022943.5, 0029872.9, 0029870.3, 0029871.1, and 0110885.1) has been granted.

**LACK OF ENABLEMENT UNDER 35 U.S.C. § 112, FIRST PARAGRAPH**

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-4, 7, 12, and 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a crystal structure of the *Thermus thermophilus* 30 S

subunit having a resolution of 3.05 Å, does not reasonably provide enablement for any 30 S subunit or any 30 S subunit having a resolution numerically less than about 3 Å. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

8. This rejection is maintained with respect to claims 1-4, 12, and 13, as recited in the previous office action mailed May 27, 2003. The instant rejection has been extended to claim 7.

### **RESPONSE TO ARGUMENT**

9. Specific to Applicant's argument via citing the instant specification, one of skill in the art would be enable to practice the claimed invention commensurate in scope with the elected claimed invention due to the high degree of conservation of the ribosome structure being known as of the filing date of the application. Applicant's argument has been fully considered and found to be unpersuasive as discussed below.

10. It is noted the pointed to disclosure supports that at the time of the instant invention it is known in the art that there is high degree of conservation of ribosome structure between prokaryotes of different species. However, the disclosure of high degree of conservation of ribosome structure between prokaryotes does not help Applicant overcome the fact that the instant specification disclose a *Thermus thermophilus* 30 S subunit having a resolution of 3.05 Å, but not any 30 S subunit that is numerically less than about 3 Å. It is noted that structure conservation is only one of many characteristics of organisms such as prokaryotes, which have been used for the classification of said organisms. It is well known in the art that

other characteristics (not a comprehensive example) such as gram stain, growth conditions, and metabolic properties have been widely used for classifying organisms of different species. Further, the knowledge of the structure of a protein is one of the many factors that contribute to the protein being able to be crystallized. Factors such as growth conditions and metabolic properties of an organism strongly determine the effort required to predictably crystallize a specific protein from said organism. It is these factors that determine the protein environment from which a protein is to be crystallized. The difference in the protein-surrounding environment due to the proteins being from organisms of different species greatly determines whether said proteins could be predictably crystallized using the same method.

11. Further, Applicant argues that the structural conservation is in the regions of structure essential for function and the function being area responsible for the interaction of the 30 S proteins with antibacterial antigens (page 11, lines 10-23). It is noted that the area of the structural conservation of proteins is not the only area of said proteins that determines whether said protein could be predictably crystallized. Even with the regions of structure essential for function being conserved, the difference in the protein sequences, due to said sequences from different species, outside of the conserved regions greatly determines whether said proteins could be predictably crystallized using the same method.

12. Therefore, it is the characteristics of structural conservation and the above-discussed factors that contribute to unpredictability of the art of protein crystallization as re-iterated below. Therefore, the citation of the high degree of conservation of ribosome structure

between prokaryotes of different species alone does enable one of skill in the art to predictably practice the claimed invention without undue experimentation.

13. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

14. It is acknowledged that the applicant has disclosed information to enable one skilled in the art to make the crystal of the *Thermus thermophilus* 30 S subunit having a resolution of 3.05 Å (Page 24, lines 28-30). However, it is well documented that protein crystallization is in essence a trial-and-error method, and the results are usually unpredictable (Drenth, J.). Further, as recently as November 1, 2002, *Science* published a New Focus article depicting the current state of the art for protein crystallization that supports the unpredictability of the art. In essences, protein crystallization is still a trial and error process because the current technology for producing protein for the crystallization process is unpredictable, which

results in high failure rate for proteins that are being crystallized. Therefore, researchers continue to have trouble generating sufficient protein required for the crystallization process (New Focus, Science, 2002). In light of the difficulty of the protein crystallization process, it is, therefore, unreasonable to expect one skilled in the art to make any 30 S subunit crystal structure or a 30 S subunit crystal structure having a resolution numerically less than about 3 A without undue experimentation.

**LACK OF WRITTEN DESCRIPTION 35 U.S.C. § 112, FIRST PARAGRAPH**

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

17. This rejection is maintained with respect to claim 12 as recited in the previous office action mailed May 27, 2003.

**RESPONSE TO ARGUMENTS**

18. Applicant contends that the disclosure of line 2 of page 5 provides adequate written description basis for a 30S subunit having a resolution less than 3 A. Applicant's argument has been fully considered and found to be unpersuasive as discussed below. It is acknowledged page 5, line 2 recites "An advantageous feature of these structures are that they diffract beyond 3 A resolution." However, the instant specification does not provide

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adequate disclosure to satisfy the Written Description requirement under 35 U.S.C. 112, First Paragraph. Due to the difficulty of the art of crystallization, a lack of adequate written description issue arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the 30S subunit having a resolution less than 3 A from the disclosed process. "To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention."

19. It is reiterated that Applicant discloses the crystal structure of the *Thermus thermophilus* 30S subunit having a resolution of 3.05 A (Pages 24, lines 28-30). However, Applicants do not provide disclosure for any 30S subunit having a resolution less than 3 A.

#### **DOUBLE PATENTING**

20. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

21. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

22. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

23. This rejection is maintained with respect to claims 1-4, 12, and 13, as recited in the previous office action mailed May 27, 2003. The instant rejection has been extended to claim 7.

24. Claims 1-4, 7, 12, and 13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of copending Application No. 09/904,779 in view of Ramakrishnan et al. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant application and the copending application claim a crystal of a 30S subunit with identical unit cell dimensions. It is acknowledged that the copending application does not claim a crystal of a 30S subunit bound to a paromomycin antibiotic as in the instant application. However, the copending application discloses, “the 30S provided by Table 1 may be used to examine and determine the binding of antibiotics such as paromomycin” (page 11, lines 23-25). One of ordinary skill in the art would have been motivated to examine the specification for the types antibiotics that bind to the 30S subunit as disclosed in the copending application. “The specification can always be used as a dictionary to learn the meaning of a term in the patent claim. Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in

the application defines an obvious variation of an invention claimed in the patent." (MPEP § 804 (II) (B) (1)) Therefore, it would have been obvious to make of crystal of a 30S subunit bound to paromomycin of the instant application.

25. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

#### **RESPONSE TO ARGUMENT**

26. Applicant responded by stating that Applicant will submit a terminal disclaimer to disclaim any portion of a patent issuing from the present application, which would extend beyond the term of a patent issuing from the 09/904,779 application, upon notification of allowable claims in the present application. Applicant's response has been acknowledged. The instant rejection has been maintained until a timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) is filed.

#### **CONCLUSION**

##### **27. NO CLAIM IS ALLOWED.**

28. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 872-9306.

29. 2. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

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30. 3. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (571) 272-0722.

31. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (571) 272-0549 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

C. Dune Ly  
2/18/04

*Ardin H. Marschel*  
ARDIN H. MARSCHEL  
PRIMARY EXAMINER